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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/713,808	11/14/2003	Dave S.B. Hoon	89212.0014	4483

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EXAMINER	
AEDER, SEAN E	
ART UNIT	PAPER NUMBER
1642	
MAIL DATE	DELIVERY MODE
04/06/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/713,808	HOON ET AL.	
	Examiner	Art Unit	
	SEAN E. AEDER	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,10,34 and 35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 10, 34, 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/6/09 has been entered.

Claims 1-7, 10, 34, and 35 are pending and are currently under consideration.

This Office Action contains New Rejections necessitated by New Considerations.

New Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5-7, 10, and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoon et al (US Patent 6,057,105; 5/2/00).

Claim 1 is drawn to a method comprising: (a) isolating nucleic acid from a sentinel lymph node (SLN) sample obtained from a melanoma patient; (b) amplifying mRNA transcripts encoded by a panel of marker genes from the nucleic acid from the SLN sample obtained from the melanoma patient wherein the panel comprises

GalNAcT, PAX3, or both; (c) detecting the levels of the mRNA transcripts encoded by the panel of marker genes in the nucleic acid from the SLN sample obtained from the melanoma patient; and (d) predicting metastatic melanoma recurrence, metastatic melanoma-free survival, overall survival, or a combination thereof for the melanoma patient. Claim 2 is drawn to the method of claim 1 wherein the panel further comprises marker genes selected from MAGE-A3 and MART-1. Claim 3 is drawn to the method of claim 2 wherein the panel comprises a first combination of MAGE-A3, GalNAcT, MART-1, and PAX3; or a second combination of MART-1, GalNAcT, and PAX3. Claim 5 is drawn to the method of claim 1 wherein the SLN sample is paraffin-embedded or frozen. Claim 6 is drawn to the method of claim 1 wherein the SLN sample is histopathologically negative for melanoma cells. Claim 7 is drawn to the method of claim 6 wherein histopathology of the SLN sample is determined by haematoxylin and eosin staining or immunohistochemistry. Claim 10 is drawn to the method of claim 1 wherein the patient's prognosis is predicted for at least a three-year period following a removal of a primary tumor, sentinel lymphadenectomy (SLND), or both. Claim 34 is drawn to a method comprising: (a) isolating nucleic acid from a blood sample obtained from a melanoma patient; (b) amplifying mRNA transcripts encoded by a panel of marker genes from the nucleic acid from the blood sample obtained from the melanoma patient wherein the panel comprises GalNAcT, PAX3, or both; (c) detecting the levels of the mRNA transcripts encoded by the panel of marker genes in the nucleic acid from the blood sample obtained from the melanoma patient; and (d) predicting metastatic

melanoma recurrence, metastatic melanoma-free survival, overall survival, or a combination thereof for the melanoma patient.

It is noted that the preambles of the instant claims are about intended purposes of the claimed methods, and the "wherein" clauses of claims 1, 10, and 34 are not active method steps. Therefore, the preambles and the "wherein" clauses of claims 1, 10, and 34 are not considered limitations to the claims.

It is further noted, that the claims require one to amplify mRNA transcripts encoded by a panel of marker genes wherein the panel comprises various recited genes. It is further noted that the claims require one to detect levels of the amplified transcripts. However, the claims do not require one to amplify or detect any particular transcript – including any of those recited in the instant claims.

Hoon et al teaches a method of detecting circulating melanoma cells comprising: (a) isolating nucleic acid from a sentinel lymph node (SLN) sample or blood sample obtained from a melanoma patient; (b) amplifying mRNA transcripts encoded by a panel of marker genes from the nucleic acid from the SLN sample or blood sample obtained from the melanoma patient wherein the panel comprises GalNAcT, PAX3, or both and the amplification is done by PCR; (c) detecting the levels of GalNAc-T, MAGE-A3, and MART-1 mRNA transcripts encoded by the panel of marker genes in the nucleic acid from the SLN sample or blood sample obtained from the melanoma patient; and (d) quantitating the melanoma status (column 41 lines 57-59, in particular), assigning a clinical melanoma stage to the subject (column 38 lines 45-51 and column 40 lines 4-6, in particular), predicting recurrence (Figure 1 and column 38 lines 60-65, in particular),

predicting survival of the subject (Figure 1, in particular), and monitoring melanoma progression or treatment response (column 21 lines 41-60 and column 14 lines 41-59, in particular) in accordance with the expression of the panel genes. The method taught by Hoon et al further comprises predicting melanoma recurrence or survival of the subject for a period of greater than 30 months following removal of a primary tumor, SLND, or both (Figure 1, in particular). The method taught by Hoon et al further comprises samples wherein the histopathology of the body fluid or tissue sample is determined by H&E and would determine whether the SLN or blood sample from the subject is histopathologically positive of negative for melanoma cells (Example VII, in particular). Hoon et al further teaches a method wherein a high number of genes expressed indicates an advanced melanoma stage, progression or melanoma, a high probability of melanoma recurrence, or a low probability of survival (Figure 1, in particular). Hoon et al further teaches a method wherein the samples are frozen (see Example VII, in particular).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7, 10, and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoon et al (US Patent 6,057,105; 5/2/00) as applied to claims 1-3, 5-7, 10, and 34 above, and further in view of Johansson et al (2000, Clinical Chemistry, 46(7): 921-927).

Teaching of claims 1-3, 5-7, 10, and 34 by Hoon et al is discussed above.

Hoon et al does not specifically teach performing qRT-PCR as the PCR method for amplifying the mRNA transcripts. However, this deficiency is made-up in the teachings of Johansson et al.

Johansson et al teaches a reproducible method comprising performing qRT-PCR to quantitatively detect mRNA markers of melanoma in biological samples (pages 922-923, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to use the qRT-PCR as the PCR method when performing the method of Hoon et al because Johansson et al demonstrates that qRT *quantitatively* detects specific numbers of transcripts which are mRNA markers of melanoma in biological samples (pages 922-923, in particular). One of ordinary skill in the art at the time the

invention was made would have had a reasonable expectation of success for using qRT-PCR as the PCR method when performing the method of Hoon et al because Johansson et al demonstrates that qRT *quantitatively* detects specific numbers of transcripts which are mRNA markers of melanoma in biological samples (pages 922-923, in particular). Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hoon et al (US Patent 6,057,105; 5/2/00) in view of Hatta et al (Melanoma Research, August 1999, 9(4): 401-406).

Claim 35 is drawn to a method comprising: (a) isolating nucleic acid from a non-sentinel lymph node (NSLN) sample obtained from a melanoma patient; (b) amplifying mRNA transcripts encoded by a panel of marker genes from the nucleic acid from the NSLN sample obtained from the melanoma patient wherein the panel comprises GalNAcT, PAX3, or both; (c) detecting the levels of the mRNA transcripts encoded by the panel of marker genes in the nucleic acid from the NSLN sample obtained from the melanoma patient; and (d) predicting metastatic melanoma recurrence, metastatic melanoma-free survival, overall survival, or a combination thereof for the melanoma patient.

Hoon et al teaches a method of detecting circulating melanoma cells comprising: (a) isolating nucleic acid from a lymph node sample obtained from a melanoma patient

(see lines 27-32 of column 3, in particular); (b) amplifying mRNA transcripts encoded by a panel of marker genes from the nucleic acid from the lymph node sample obtained from the melanoma patient wherein the panel comprises GalNAcT, PAX3, or both and the amplification is done by PCR; (c) detecting the levels of GalNAc-T, MAGE-A3, and MART-1 mRNA transcripts encoded by the panel of marker genes in the nucleic acid from the lymph node sample obtained from the melanoma patient; and (d) quantitating the melanoma status (column 41 lines 57-59, in particular), assigning a clinical melanoma stage to the subject (column 38 lines 45-51 and column 40 lines 4-6, in particular), predicting recurrence (Figure 1 and column 38 lines 60-65, in particular), predicting survival of the subject (Figure 1, in particular), and monitoring melanoma progression or treatment response (column 21 lines 41-60 and column 14 lines 41-59, in particular) in accordance with the expression of the panel genes.

Hoon et al does not specifically teach a method wherein the lymph node sample is a “non-sentinel" lymph node (NSLN) sample. However, this deficiency is made up in the teachings of Hatta et al.

Hatta et al teaches methods of detecting circulating melanoma cells in non-sentinel lymph nodes comprising using RT-PCR to amplify markers expressed by circulating melanoma cells (see abstract).

One of ordinary skill in the art at the time the invention was made would have been motivated to use a "non-sentinel" lymph node sample as the lymph node sample when performing the method of Hoon et al because Hatta et al teaches circulating melanoma cells are found in non-sentinel lymph nodes and can be detected by using

RT-PCR to amplify markers expressed by circulating melanoma cells (see abstract). One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for using a "non-sentinel" lymph node sample as the lymph node sample when performing the method of Hoon et al because Hatta et al teaches circulating melanoma cells are found in non-sentinel lymph nodes and can be detected by using RT-PCR to amplify markers expressed by circulating melanoma cells (see abstract). Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 35 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a **NEW MATTER** rejection.

Claims 35 recites method comprising: (a) isolating nucleic acid from a non-sentinel lymph node (NSLN) sample obtained from a melanoma patient; (b) amplifying mRNA transcripts encoded by a panel of marker genes from the nucleic acid from the

NSLN sample obtained from the melanoma patient wherein the panel comprises GalNAcT, PAX3, or both; (c) detecting the levels of the mRNA transcripts encoded by the panel of marker genes in the nucleic acid from the NSLN sample obtained from the melanoma patient; and (d) predicting metastatic melanoma recurrence, metastatic melanoma-free survival, overall survival, or a combination thereof for the melanoma patient. Descriptions of method comprising: (a) isolating nucleic acid from a non-sentinel lymph node (NSLN) sample obtained from a melanoma patient; (b) amplifying mRNA transcripts encoded by a panel of marker genes from the nucleic acid from the NSLN sample obtained from the melanoma patient wherein the panel comprises GalNAcT, PAX3, or both; (c) detecting the levels of the mRNA transcripts encoded by the panel of marker genes in the nucleic acid from the NSLN sample obtained from the melanoma patient; and (d) predicting metastatic melanoma recurrence, metastatic melanoma-free survival, overall survival, or a combination thereof for the melanoma patient are not found in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the invention was filed, had possession of the claimed invention.

In the Reply of 7/30/07, Applicant argued that the invention is directed in part to detection of micro metastasis in cancerous lymph nodes using qRT-PCR (see, e.g., lines 12-14 on page 2 of the specification) and that the specification indicates that lymph nodes include both sentinel lymph nodes (SLN) and non-sentinel lymph nodes (NSLN) (see,.e.g., lines 15-24 on page 3 of the specification). Applicant further argues that one

of skill in the art would understand that NSLN can be used in the methods of the invention just like SLN.

Upon further careful consideration, the arguments found in the Reply of 7/30/07 are not deemed persuasive. While the specification and the originally filed claims disclose methods directed in part to detection of micro metastasis in cancerous lymph nodes using qRT-PCR and the specification indicates that lymph nodes include both sentinel lymph nodes (SLN) and non-sentinel lymph nodes (NSLN), the specification does not express inherent or implicit support for methods of detecting micro metastasis in NSLN as claimed. Further, lines 21-26 on page 3 of the specification state that the disclosed method of detecting micro metastasis in SLN samples allows one to avoid complete lymph node dissection and various postoperative complications associated with such a procedure because the probability of NSLN containing melanoma cells is less than 1% when the SLN does not have metastatic melanoma cells. Therefore, the specification provides clear guidance that the claimed method is *not* to be performed using NSLN samples.

Summary

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SEAN E. AEDER whose telephone number is (571)272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sean E Aeder/
Primary Examiner, Art Unit 1642